

## [54] MODIFIED NUCLEOTIDES AND METHODS OF PREPARING AND USING SAME

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### Related U.S. Application Data

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536/24; 536/26; 536/27; 536/28  
[58] Field of Search ..... 536/27, 28, 29, 26,  
536/24, 23; 435/5, 6

### [56] References Cited

#### U.S. PATENT DOCUMENTS

3,328,389	6/1967	Shimizu et al.	260/211.5
3,337,530	8/1967	Hanze	260/211.5
3,338,882	8/1967	Wechter	260/211.5
3,804,826	4/1974	Schelt et al.	260/211.5 R
3,893,998	7/1975	Secrist, III et al.	260/211.5 R
3,915,958	10/1975	Shuman et al.	260/211.5 R
3,917,583	11/1975	Meyer et al.	260/211.5 R
3,960,840	6/1976	Secrist, III et al.	260/211.5 R
3,968,101	7/1976	Christensen et al.	260/211.5 R
4,008,363	2/1977	Re et al.	536/28
4,038,480	7/1977	Robins et al.	536/27
4,048,307	9/1977	Yokota et al.	424/180
4,086,417	4/1978	Ishida et al.	536/29
4,088,639	5/1978	Zapelli et al.	260/112.5 R
4,096,324	6/1978	Kelly et al.	536/23
4,134,792	1/1979	Boguslaski et al.	195/99
4,151,349	4/1979	Traeger et al.	536/28
4,171,432	10/1979	Carrico et al.	536/26
4,213,893	7/1980	Carrico et al.	260/112.5
4,228,237	10/1980	Hevey et al.	435/7
4,230,698	10/1980	Bobek et al.	424/180
4,230,797	10/1980	Boguslaski et al.	435/7

(List continued on next page.)

#### FOREIGN PATENT DOCUMENTS

070685	1/1983	European Pat. Off.	.
70687	1/1983	European Pat. Off.	.
2618419	11/1976	Fed. Rep. of Germany	.
2618511	11/1976	Fed. Rep. of Germany	.
3045375	7/1982	Fed. Rep. of Germany	.
18-24191	10/1943	Japan	.
58-62194	4/1983	Japan	.
8302276	7/1983	PCT Int'l Appl.	.
8302277	7/1983	PCT Int'l Appl.	.
8302286	7/1983	PCT Int'l Appl.	.
1548741	7/1979	United Kingdom	.
1552607	9/1979	United Kingdom	.
2019408	10/1979	United Kingdom	.
2026690	2/1980	United Kingdom	.
2034323	6/1980	United Kingdom	.
2041922	9/1980	United Kingdom	.
2045239	10/1980	United Kingdom	.
2125964	3/1984	United Kingdom	.

### OTHER PUBLICATIONS

J. G. J. Bauman et al., "A New Method for Fluorescence Microscopical Localization of Specific DNA Sequences by In Situ Hybridization of Fluorochrome-Labelled RNA", *Exp. Cell Res.* 128, pp. 485-490 (1980).

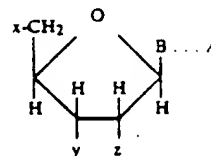
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### [57] ABSTRACT

Compounds having the structure:

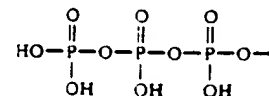
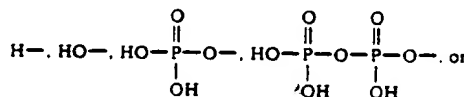


wherein B represents a purine, 7-deazapurine, or pyrimidine moiety covalently bonded to the C1'-position of the sugar moiety, provided that when B is purine or 7-deazapurine, it is attached at the N9-position of the purine or 7-deazapurine and when B is pyrimidine, it is attached at the N1-position;

wherein A represents a moiety consisting of at least three carbon atoms which is capable of forming a detectable complex with a polypeptide when the compound is incorporated into a double-stranded ribonucleic acid, deoxyribonucleic acid duplex, or DNA-RNA hybrid;

wherein the dotted line represents a chemical linkage joining B and A, provided that if B is purine, the linkage is attached to the 8-position of the purine, if B is 7-deazapurine, the linkage is attached to the 7-position of the deazapurine, and if B is pyrimidine, the linkage is attached to the 5-position of the pyrimidine and

wherein each of x, y and z represents



either directly, or when incorporated into oligo- and polynucleotides, provide probes which are widely useful.

Applications include detection and localization of polynucleotide sequences in chromosomes, fixed cells, tissue sections, and cell extracts. Specific applications include chromosomal karyotyping, clinical diagnosis of nucleic acid-containing etiological agents, e.g. bacteria, viruses, or fungi, and diagnosis of genetic disorders.